

### In the Specification

Please amend the specification begin on page three line 28 through page 7, line 5 as follows.

### BRIEF DESCRIPTION OF THE DRAWINGS DESCRIPTION OF RESULTS

~~Fig. 1 shows graphs of a~~ A study of basal transmission and paired-pulse facilitation (PPF) was graphed to provide. ~~Fig. 1a, top, graphs are~~ examples of field responses and hippocampal slice CA1 region evoked by delivery of increasing intensity stimuli for wild-type (“wt”) and  $\Delta 9$  mutant animals (averages of 5 each). ~~Figure 1a bottom is~~ A graph was made of the input-output plot of basal transmission in mutant ( $\Delta$ ) and wt animals ( $\bigcirc$ ) obtained from responses evoked as ~~in 1a (top) above~~. The plot includes data from 4 wt and 6 mutant slices. Best fit line to each group (linear regression) shows slopes that are not significantly different ( $p > 0.05$ ). ~~Scale bars: 10 ms and 0.2 mv.~~ ~~Fig. 1b top~~ A graph was made which shows examples of responses to paired stimuli (50 ms inter-stimulus interval, averages of 10 each). ~~Fig. 1b bottom~~ A graph was made which is a plot of percent potentiation versus inter-pulse interval for mutant ( $\Delta$ , n=6 slices) and wt ( $\bigcirc$ , n=6 slices) animals. Values and not significantly different ( $p > 0.05$ ). ~~Scale bars: 50 ms and 0.1 mv.;~~

~~Fig. 2 shows graphs~~ Graphs were made of epsp response to tetani in the presence or absence of agents which affect the role of GABA<sub>A</sub> receptor to evaluate the role of GABA<sub>A</sub> in the presence or absence of agents , which affect the GABA<sub>A</sub> receptor. ~~Fig. 2a graphs~~ Data are based on experiments with GABA<sub>A</sub> transmission intact. ~~On the left, Data include~~ examples of epsp response (averages of 10 each) immediately before and 20 min after a tetanus superimposed for wt and mutant animals. ~~Scale bars: 0.2 mV and 20 ms apply to a and b.~~ ~~On the right, The graphs include~~ a plot of mean epsp slope (+/- SEM) normalized to values before a tetanic stimulus (time 0). For each slice transmission to independent pathways were monitored. Tetanized pathway showed greater enhancement in slices from mutant (~~open triangles~~, n=8 slices) than wt (~~open circles~~, n=10 slices) animals. Control pathways (mutant, ~~closed triangles~~; and wt ~~closed circles~~)

remained unchanged. Tetanus consisted of 100 stimuli delivered over 1 sec (100 Hz). The potentiation at the time points of 5, 10, 15, 20, 25 and 30 min was:  $1.36 \pm 0.060$ ,  $1.26 \pm 0.058$ ,  $1.27 \pm 0.054$ ,  $1.24 \pm 0.058$ ,  $1.22 \pm 0.063$  and  $1.21 \pm 0.069$ , respectively for the wt. for the same time points for the mutant these values were:  $1.67 \pm 0.065$ ,  $1.52 \pm 0.054$ ,  $1.54 \pm 0.072$ ,  $1.56 \pm 0.075$ ,  $1.51 \pm 0.089$  and  $1.54 \pm 0.090$ , respectively. At these time points, ~~there~~ there was a statistically significant difference between the two sets of data points ( $< 0.05$ ). ~~Abbreviation “PTX”, no picrotoxin in the bath.~~ Fig. 2b A graph was made which shows results with GABA<sub>A</sub> transmission blocked with 100  $\mu$ M picrotoxin. ~~On the left,~~ Data are examples of epsp responses (averages 10 each) . immediately before and 20 min after a tetanus superimposed for wt (~~top~~) and mutant (~~bottom~~) animals. ~~On the right,~~ Data are a plot of mean epsp slope  $\pm$  SEM normalized to values before tetanic stimulus (time 0). For these experiments, control pathways were monitored for only 30 min after tetanus. Tetanized pathways showed similar enhancement in slices from mutant (~~open triangle~~,  $n=13$  slices) and wt (~~open circles~~,  $n=18$  slices) animals. Control pathways (~~mutant, closed triangles and wt closed circles~~) remained unchanged. Tetanus consisted of 25 pulses given as groups of 5 pulses and 100 Hz every 10 s, 5 times. This tetanus was weaker than in Fig. 2a above to obviate possible differences between wt and mutant induction. ~~Abbreviation “+PTX”, with picrotoxin in bath.~~ Fig. 2c ~~shows~~ Data were developed and graphed which showed the results of experiments in the presence of N-methyl-D-aspartate (NMDA)-receptor blockade with AP5. Plot of mean epsp slope  $\pm$  SEM normalized to values before tetanic stimulus (time 0).;

~~Fig. 3 shows~~ Data were developed and graphed which showed the effect of flunitrazepam on LTP. Fig. 3a ~~is~~ Data were prepared as a graph of the means  $\pm$  SEM of normalized epsp responses and the absence of drug plotted against time: ( $\clubsuit$ ,  $n=7$  slices), and  $\Delta 9$  mutation ( $\blacktriangle$ ,  $n=12$  slices). There was a significantly greater amount of potentiation in the mutant at the time points of 5, 10 and 15 min post-tetanus. At 20 min, the difference in potentiation became insignificant. The tetanus (delivered at time 0) was 100 pulses given for 1 s (100 Hz) every 20 s 3x in succession. Control pathways (receiving no tetanus) remained unchanged. ~~Abbreviation”~~

FLU.", no flunitrazepam in bath. Fig. 3b was as in Fig. 3a but in the presence of flunitrazepam in the bathing medium; (●, n=11 slices) and  $\Delta 9$  mutation (▲, n=8 slices). There was no statistically significant difference between the two groups at the above time points post-tetanus. Control pathways (receiving no tetanus) remained unchanged. Abbreviation: FLU.", flunitrazepam present in bath. Fig. 3c is the same data as Figs. 3a and 3b comparing Comparing potentiation in mutants (+FLU) with the wt (-FLU) to show shows the suppression of the each the potentiation to almost the wt levels. Fig. 3d are histograms from the data of Figs. 4a and 4b Histograms were prepared from the data of the following paragraph and showed potentiation at various times post-tetanus. All groups were compared with each other, only statistically significantly and the statistical significance of the different pairs ( $p < 0.05$ ) are shown by the lines determined. These comparisons were calculated for 5 min, 10 min (histogram not shown) and 15 min. These time points gave identical statistical results for pairwise comparisons as in the 5 min case. For the 20 min time point, however, the W vs. M comparison was not significant but the other two pairwise group comparisons were significant at ( $p < 0.05$ ). W=wild type, M=mutant, Wf=wt+FLU, Mf=mutant+FLU.;

Fig. 4 are Data were prepared as graphs of the effect of agents on the GABA<sub>A</sub> receptor-mediated transmission in the mutant and wt cells using whole-cell patch-clamping. Fig. 4a graphs The data included the evoked synaptic response (averaged up to 20 each) from whole-cell patch-clamped neurons. Output current recorded at 0mV is completely blocked by 100  $\mu$ M PTX, a GABA<sub>A</sub> receptor antagonist. NBQX blocked some of the output current (not shown), indicating some disynaptic inhibition. At the holding potential of -60mV, the Inwood current is completely blocked with 2  $\mu$ M NBQX, the AMPA (glutamate subtype) receptor blockade. Scale bar: 25pA and 20ms. Fig. 4b graphs the The evoked synaptic responses (averaged up to 15 each) were recorded at holding potentials of 0mV and -60mV with the stimulating electrode placed in stratum radiatum (top) and site 1, 50  $\mu$ m from the recording electrode (middle) and site 2, ~250  $\mu$ m from the recording electrode and (bottom) at site two with the stimulus intensity increased ~3-fold. Scale bars: top 50pA; middle, 100 pA; bottom, 50 pA; time scale, as in Fig. 4a. Fig. 4c, left,

Graphs were prepared of examples of averaged (up to 15 each) traces from patch-clamp whole-cell recordings in wt and  $\Delta 9$  mutation at -60mV (glutamate currents) and at 0mV (GABA<sub>A</sub> currents). Scale bar: 40pA and 20ms. On the right, The graphs included peak amplitude of response ratios (measured at holding potentials of -60mV and 0mV, respectively) from cells in individual slices (n=9 slices each). ~~The means $\pm$ SEM are also shown and superimposed using the filled symbols.~~ The ratios are significantly greater in the mutant than in the wt ( $p < 0.05$ , t-test).

~~Fig. 5 graphs~~ Also graphed were the results from the effects of AP5-sensitive potentials during tetanus. One of the graphs show's normalized traces of field potential response to four consecutive (every 10ms) stimuli, before (the larger response) and after (the intermediate response) the application of the specific NMDA-receptor antagonist, AP5. ~~The differences between the two responses at each time point are also shown.~~ The responses were normalized to the area up to the peak of the first response (which is mostly due to non-NMDA receptor activation). ~~Scale bar: 10ms.~~ Fig. 5b Another graph shows the averaged differences of areas under the four response curves, before and after AP5 application in individual (wt and  $\Delta 9$  mutant) slices to show the effect of tetanus on the NMDA (or AP5)-sensitive component. ~~The means $\pm$ SEM of all slices are also shown in filled symbols.~~ Although the mean AP5-sensitive potentials were smaller in mutants (despite manifesting a greater potentiation (see Fig. 2)), there was no statistically significant difference between the two groups.